

REMARKS

The present amendment is made to eliminate multiple dependent claims and thus eliminate the requirement for a multiple dependent claim fee and to add an Abstract of the Disclosure to conform with U.S. practice.

Respectfully submitted,

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By: Douglas E. Jackson  
Registration No.: 28,518

**LARSON & TAYLOR, PLC • 1199 North Fairfax St. • Suite 900 • Alexandria, VA 22314 • (703) 739-4900**

## ATTACHMENT A

### Clean Replacement/New Claims (entire set of pending claims)

*Following herewith is a clean copy of the entire set of pending claims.*

1. A process for preparing a crosslinked collagenic material which is biocompatible and nontoxic and has a controlled *in vivo* rate of biodegradation, characterized in that it comprises subjecting a collagenic component substantially free of any complementary crosslinking agent, and preferably not crosslinked, in the wet state to irradiation by beta rays, the collagenic material obtained being sterile and biodegradable over a few days to several weeks.
2. The process as claimed in claim 1, characterized in that the collagenic compound has a moisture content of greater than 30%, preferably greater than 40%.
3. (AMENDED) The process as claimed in claim 1, characterized in that the collagenic component is in the form of a gel.
4. (AMENDED) The process as claimed in claim 1, characterized in that the collagenic component is in the form of an aqueous solution.
5. (AMENDED) The process as claimed in claim 1, characterized in that the collagenic component has a neutral pH, preferably between 6.5 and 8.
6. (AMENDED) The process as claimed in claim 1, characterized in that the concentration of the collagenic component (solids content) is a minimum of 0.5% and preferably greater than 2.5%.

cont.  
A1

7. (AMENDED) The process as claimed in claim 1, characterized in that the collagenic component consists of or comprises collagen that has at least partially lost its helical structure.
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8. The process as claimed in claim 7, characterized in that the collagen that has at least partially lost its helical structure is formed from unhydrolyzed collagen consisting mostly of  $\alpha$  chains.
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9. (AMENDED) The process as claimed in claim 7, characterized in that the collagenic component consists of or comprises collagen that has at least partially lost its helical structure by heating above 37°C, preferably between 40 and 50°C.
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A2

10. (AMENDED) The process as claimed in claim 1, characterized in that the collagenic component consists of or comprises oxidized collagen.
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11. The process as claimed in claim 10, characterized in that the oxidized collagen consists of collagen modified by oxidative scission using periodic acid or one of its salts.
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12. (AMENDED) The process as claimed in claim 1, characterized in that the collagenic component comprises collagen functionalized at the level of the amino and/or carboxyl functional groups of the amino acids.
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A3

13. (AMENDED) The process as claimed in claim 1, characterized in that the collagenic component comprises a macromolecular hydrophilic additive.
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14. The process as claimed in claim 12, characterized in that the macromolecular hydrophilic additive has a molecular weight greater than 3 000 daltons.
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15. (AMENDED) The process as claimed in claim 13, characterized in that the macromolecular hydrophilic additive is a hydrophilic polymer having a molecular weight of between 3 000 and 20 000 daltons.

16. (AMENDED) The process as claimed in claim 13, characterized in that the macromolecular hydrophilic additive is polyethylene glycol.

17. (AMENDED) The process as claimed in claim 13, characterized in that the macromolecular hydrophilic additive is chosen from polysaccharides, especially starch, dextran and cellulose, or mucopolysaccharides.

18. The process as claimed in claim 17, characterized in that the macromolecular hydrophilic additive is a polysaccharide in oxidized form.

19. The process as claimed in claim 1, characterized in that the collagenic component is irradiated with a dose of 5 to 50 kGy.

20. (AMENDED) The process as claimed in claim 19, characterized in that the collagenic component is irradiated with a dose of 20 to 50 kGy, preferably 25 to 35 kGy.

21. (AMENDED) The process as claimed in claim 1, characterized in that the collagenic component is irradiated by beta rays, the resulting collagenic material being highly crosslinked and biodegradable *in vivo* over several weeks.

22. (AMENDED) The process as claimed in claim 1, characterized in that the collagenic component in the wet state is combined with a network of collagen fibers preferably of helical structure, prior to its irradiation.

23. The process as claimed in claim 22, characterized in that the network of collagen fibers consists of a compress of compacted fibers, obtained from an acid solution of native collagen, by treatment using periodic acid or one of its salts, formation

of fibers and then crosslinking by neutralization, the resulting crosslinked collagen fibers of helical structure being compressed by applying pressure, and in that a solution of a collagenic component is deposited on said compress and then the assembly is irradiated by beta rays.

24. A collagenic bicomposite which is biocompatible, nontoxic and sterile, has a controlled *in vivo* rate of biodegradation and is able to be applied by sutures or staples, characterized in that it comprises only, or mainly, two layers intimately associated and crosslinked with interpenetration of the crosslinked networks, one of said layers being formed from a film based on a crosslinked collagenic component and the other from a compacted compress formed from crosslinked collagen fibers rendered insoluble, especially collagen fibers having a helical structure, prepared from collagen dissolved or dispersed in an aqueous solution.

25. (AMENDED) The collagenic bicomposite as claimed in claim 24, characterized in that it is crosslinked by the process characterized in that the collagenic component in the wet state is combined with a network of collagen fibers preferably of helical structure, prior to its irradiation.

26. (AMENDED) The collagenic bicomposite as claimed in claim 24, characterized in that the collagenic component comprises one of (a) collagen that has at least partially lost its helical structure, (b) oxidized collagen, or (c) a macromolecular hydrophilic additive.

## ATTACHMENT B

### Marked Up Replacement Claims

*Following herewith is a marked up copy of each rewritten claim together with all other pending claims.*

1. A process for preparing a crosslinked collagenic material which is biocompatible and nontoxic and has a controlled *in vivo* rate of biodegradation, characterized in that it comprises subjecting a collagenic component substantially free of any complementary crosslinking agent, and preferably not crosslinked, in the wet state to irradiation by beta rays, the collagenic material obtained being sterile and biodegradable over a few days to several weeks.
2. The process as claimed in claim 1, characterized in that the collagenic compound has a moisture content of greater than 30%, preferably greater than 40%.
3. (AMENDED) The process as claimed in ~~either of claims 1 and 2~~ claim 1, characterized in that the collagenic component is in the form of a gel.
4. (AMENDED) The process as claimed in ~~either of claims 1 and 2~~ claim 1, characterized in that the collagenic component is in the form of an aqueous solution.
5. (AMENDED) The process as claimed in ~~any one of the preceding claims~~ claim 1, characterized in that the collagenic component has a neutral pH, preferably between 6.5 and 8.
6. (AMENDED) The process as claimed in ~~any one of the preceding claims~~ claim 1, characterized in that the concentration of the collagenic component (solids content) is a minimum of 0.5% and preferably greater than 2.5%.

7. (AMENDED) The process as claimed in ~~any one of the preceding claims~~ claim 1, characterized in that the collagenic component consists of or comprises collagen that has at least partially lost its helical structure.
8. The process as claimed in claim 7, characterized in that the collagen that has at least partially lost its helical structure is formed from unhydrolyzed collagen consisting mostly of  $\alpha$  chains.
9. (AMENDED) The process as claimed in ~~either of claims 7 and 8~~ claim 7, characterized in that the collagenic component consists of or comprises collagen that has at least partially lost its helical structure by heating above 37°C, preferably between 40 and 50°C.
10. (AMENDED) The process as claimed in ~~any one of claims 1 to 6~~ claim 1, characterized in that the collagenic component consists of or comprises oxidized collagen.
11. The process as claimed in claim 10, characterized in that the oxidized collagen consists of collagen modified by oxidative scission using periodic acid or one of its salts.
12. (AMENDED) The process as claimed in ~~any one of claims 1 to 6~~ claim 1, characterized in that the collagenic component comprises collagen functionalized at the level of the amino and/or carboxyl functional groups of the amino acids.
13. (AMENDED) The process as claimed in ~~any one of the preceding claims~~ claim 1, characterized in that the collagenic component comprises a macromolecular hydrophilic additive.
14. The process as claimed in claim 12, characterized in that the macromolecular hydrophilic additive has a molecular weight greater than 3 000 daltons.

15. (AMENDED) The process as claimed in ~~either of claims 13 and 14~~ claim 13, characterized in that the macromolecular hydrophilic additive is a hydrophilic polymer having a molecular weight of between 3 000 and 20 000 daltons.
16. (AMENDED) The process as claimed in ~~any one of claims 13 to 15~~ claim 13, characterized in that the macromolecular hydrophilic additive is polyethylene glycol.
17. (AMENDED) The process as claimed in ~~any one of claims 13 to 16~~ claim 13, characterized in that the macromolecular hydrophilic additive is chosen from polysaccharides, especially starch, dextran and cellulose, or mucopolysaccharides.
18. The process as claimed in claim 17, characterized in that the macromolecular hydrophilic additive is a polysaccharide in oxidized form.
19. The process as claimed in ~~any one of the preceding claims~~ claim 1, characterized in that the collagenic component is irradiated with a dose of 5 to 50 kGy.
20. (AMENDED) The process as claimed in ~~any one of the preceding claims~~ claim 19, characterized in that the collagenic component is irradiated with a dose of 20 to 50 kGy, preferably 25 to 35 kGy.
21. (AMENDED) The process as claimed in ~~any one of the preceding claims~~ claim 1, characterized in that the collagenic component is irradiated by beta rays, the resulting collagenic material being highly crosslinked and biodegradable *in vivo* over several weeks.



22. (AMENDED) The process as claimed in ~~any one of the preceding claims~~ claim 1, characterized in that the collagenic component in the wet state is combined with a network of collagen fibers preferably of helical structure, prior to its irradiation.
23. The process as claimed in claim 22, characterized in that the network of collagen fibers consists of a compress of compacted fibers, obtained from an acid solution of native collagen, by treatment using periodic acid or one of its salts, formation of fibers and then crosslinking by neutralization, the resulting crosslinked collagen fibers of helical structure being compressed by applying pressure, and in that a solution of a collagenic component is deposited on said compress and then the assembly is irradiated by beta rays.
24. A collagenic bicomposite which is biocompatible, nontoxic and sterile, has a controlled *in vivo* rate of biodegradation and is able to be applied by sutures or staples, characterized in that it comprises only, or mainly, two layers intimately associated and crosslinked with interpenetration of the crosslinked networks, one of said layers being formed from a film based on a crosslinked collagenic component and the other from a compacted compress formed from crosslinked collagen fibers rendered insoluble, especially collagen fibers having a helical structure, prepared from collagen dissolved or dispersed in an aqueous solution.
25. (AMENDED) The collagenic bicomposite as claimed in claim 24, characterized in that it is crosslinked by the process ~~according to either of claims 22 and 23~~ characterized in that the collagenic component in the wet state is combined with a network of collagen fibers preferably of helical structure, prior to its irradiation.
26. (AMENDED) The collagenic bicomposite as claimed in ~~either of claims 24 and 25~~ claim 24, characterized in that the collagenic component ~~is as defined in any one of claims 7 to 18~~ comprises one of (a) collagen that has at least partially lost its helical structure, (b) oxidized collagen, or (c) a macromolecular hydrophilic additive.